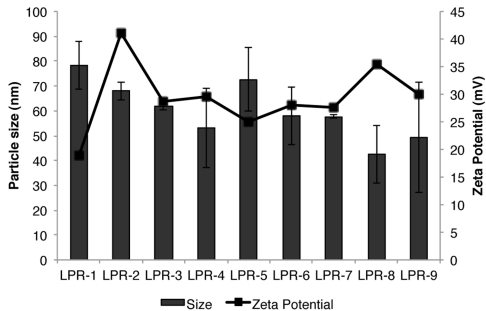


Supplementary Text and Figures

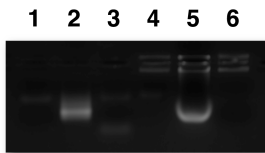
a

	1x DOTAP/ Cholesterol	2x DOTAP/ Cholesterol	3x DOTAP/ Cholesterol
1x Protamine	LPR-1	LPR-4	LPR-7
2x Protamine	LPR-2	LPR-5	LPR-8
3x Protamine	LPR-3	LPR-6	LPR-9

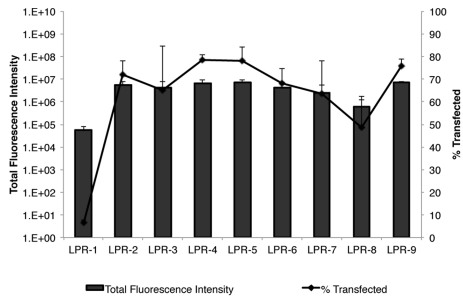
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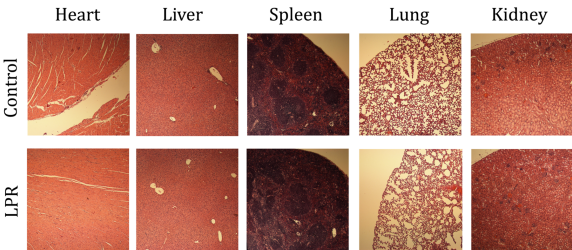
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d



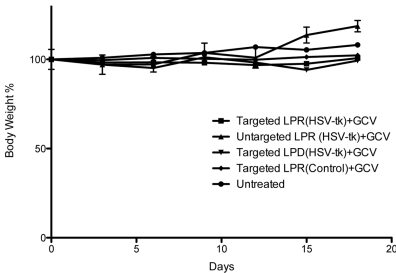
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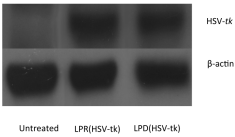
f

	BUN	AST	ALT
PBS treated	16±2.8	140.5±10.6	55.5±9.1
LPR treated	23±2.3	189±20	51.7±0.9
Normal Range	8~33	54~298	17~77

g



h



Supplementary Materials: (a) Matrix showing the designation of LPR formulation in each combination of various amounts of protamine and DOTAP/cholesterol. Different amounts of protamine and DOTAP/chol liposome were used to complex with mRNA to form LPR nanoparticles. The number indicated the charge ratio (N/P ratio) between the cationic liposomes used (or protamine) and anionic nucleic acids. **(b) Particle size and zeta potential characterization with various formulations.** The data are reported as mean \pm SD. **(c) Gel retardation assay of mRNA and LPR complexes.** Naked mRNA or LPR particles were incubated with 10% serum before loaded on a 0.7% agarose gel. 1) Serum sample is loaded for background control; 2) Untreated naked mRNA is loaded as a positive control; 3) Naked mRNA was incubated with serum before loaded on the gel; 4) LPR was incubated with serum before loaded; 5) LPR was firstly incubated with serum and then decomplexed with SDS before loaded on the gel; 6) Untreated LPR loaded as a control. **(d) Quantification of LPR-mediated H460 transfection efficiency.** Percent of transfected cells and total green fluorescent protein expression for the H460 cells transfected with nanoparticles at various formulations. The data were reported as mean \pm SD. **(e) H&E staining of major organs from CD-1 mice that received multiple doses of LRP.** **(f) Hepatocytotoxicity and renal toxicity determined by AST/ALT and BUN respectively after repetitive systemic administration of LPR to CD-1 mice.** **(g) Monitoring of animal weight during the treatment.** All the values were normalized based on the initial weight of the animals from corresponding group. The data were reported as mean \pm SD. **(h) Western Blot analysis of homogenates of tumors from animals that received treatment of**

LPR or LPD nanoparticles. HSV-tk was blotted for the confirmation of expression and the expression level was compared as β -actin was blotted as a loading control.